

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020241/S003 AND 020764/S001

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

Time Sensitive Patent Information

pursuant to 21 C.F.R. § 314.53
for
LAMICTAL® (lamotrigine) Tablets

NDA 20-241

The following is provided in accord with the Drug Price Competition and Patent Term Restoration Act of 1984:

Trade Name:	LAMICTAL® Tablets
Active Ingredient(s):	lamotrigine
Strength(s):	25mg, 50mg, 100mg, 150mg, 200mg and 250mg
Dosage Form:	Tablets
NDA Number:	20-241
Approval Date:	December 27, 1994

U.S. Patent 4,602,017

Expiration Date:	July 22, 2008 <ul style="list-style-type: none">• The original expiration date of July 22, 2003 has been extended 5 years pursuant to 35 U.S.C. § 156.
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Type of Patent:	Drug Product <ul style="list-style-type: none">• Formulation / Composition Method of Use <ul style="list-style-type: none">• Method of treating epilepsy
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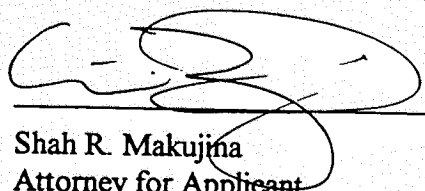
Name of Patent Owner:	Glaxo Wellcome Inc.
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The undersigned declares that U.S. Patent 4,602,017 covers the formulation, composition and/or method of use of LAMICTAL® (lamotrigine) Tablets. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act. Please address all communications to:

David J. Levy, Ph.D.
Patent Counsel
Glaxo Wellcome Inc.
Intellectual Property Department
Five Moore Drive
Research Triangle Park, NC 27709
(919) 483-7656

Respectfully submitted by:
Glaxo Wellcome Inc.

October 15, 1996
Date


Shah R. Makujina
Attorney for Applicant
Glaxo Wellcome Inc.

Patent Information

pursuant to 21 C.F.R. § 314.53
for
LAMICTAL® (lamotrigine) Chewable Dispersible Tablets

NDA 20-764

The following is provided in accord with the Drug Price Competition and Patent Term Restoration Act of 1984:

Trade Name:	LAMICTAL® Chewable Dispersible Tablets
Active Ingredient(s):	lamotrigine
Strength(s):	5mg, 25mg and 100mg
Dosage Form:	Tablets
NDA Number:	20-764
Approval Date:	Pending

U.S. Patent 5,698,226

Expiration Date:	January 29, 2012
	<ul style="list-style-type: none">• 20 years from the filing of PCT/GB/00163 which issued as U.S. 5,556,639 of which U.S. 5,698,226 is a divisional of thereof.

Type of Patent:	Drug Product
	<ul style="list-style-type: none">• Formulation / Composition

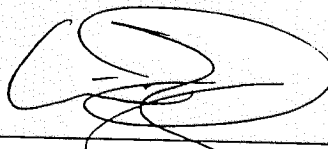
Name of Patent Owner:	Glaxo Wellcome Inc.
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The undersigned declares that U.S. Patent 5,698,226 covers the formulation, composition and/or method of use of LAMICTAL® (lamotrigine) Chewable Dispersible Tablets. This product is the subject of this application for which approval is being sought. Please address all communications to:

David J. Levy, Ph.D.
Patent Counsel
Glaxo Wellcome Inc.
Intellectual Property Department
Five Moore Drive
Research Triangle Park, NC 27709
(919) 483-7656

Respectfully submitted by:
Glaxo Wellcome Inc.

January 12, 1997
Date


Shah R. Makujina
Attorney for Applicant
Glaxo Wellcome Inc.

Exclusivity Summary Form
(Modified: October 14, 1998)

EXCLUSIVITY SUMMARY FOR NDA # 20-241

SUPPL # SE1-003

Trade Name: Lamictal Tablets

Generic Name: lamotrigine

Applicant Name: Glaxo Wellcome

HFD #: HFD-120

Approval Date If Known: _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?
YES/___/ NO / X /

b) Is it an effectiveness supplement?
YES / X / NO / ___ /

If yes, what type? (SE1, SE2, etc.) SE1

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / X / NO / ___ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

Form OGD-011347

cc: Original NDA Division File HFD-93 Mary Ann Holovac

- d) Did the applicant request exclusivity?
YES / ☒ / NO / ☐ /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

With the original submission of NDA 20-241/S-003 on 2/24/97, Glaxo Wellcome requested three years of exclusivity from the data of approval of Lamictal as monotherapy for the treatment of partial seizures in adults with epilepsy. [For completeness, a copy of the 2/25/97 request is attached to the end of this exclusivity summary.]

- e) Has pediatric exclusivity been granted for this Active Moiety?
YES / ☐ / NO / ☒ /

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO - please indicate as such)

YES / ☐ / NO / ☒ /

If yes, NDA # _____. Drug Name _____.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?
YES / ☐ / NO / ☒ /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

APPEARS THIS WAY
ON ORIGINAL

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / X / NO / /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#: NDA 20-241/Lamictal (lamotrigine) Tablets
NDA 20-764/Lamictal (lamotrigine) Chewable Dispersible Tablets

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES / / NO / X /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS.

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations?
(The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) **If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a).** If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / ☒ / NO / ☐ /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / ☒ / NO / ☐ /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8.**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / ☒ / NO / ☐ /

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.
YES / ☐ / NO / ☒ /

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES / ☐ / NO / ☒ /

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study US 30/31, titled "A Multicenter, Double-Blind, Active-Control Evaluation of the Efficacy and Safety of Lamotrigine Monotherapy in Patients with Partial Seizures", was submitted by Glaxo Wellcome in support of FDA approval of these supplemental applications.

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES / ☐ / NO / ☒ /

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

(b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES / ☐ / NO / ☒ /

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study US 30/31

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1: Study US 30/31

YES / ☒ / NO / ☐ / Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Not Applicable.

Investigation #1: YES / ☐ / Explain _____ NO / ☐ / Explain _____

Investigation #2: YES / ☐ / Explain _____ NO / ☐ / Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES / ☐ / NO / ☒ /

If yes, explain: _____

Signature of Preparer: _____

/S/

Date: 12/23/98

Title: _____

Regulatory Management Officer

Signature of Division Director _____

/S/

Signature: _____

Date: 12/23/98

cc:

Original NDA

Division File

HFD-93 Mary Ann Holovac

**APPEARS THIS WAY
ON ORIGINAL**

Exclusivity Summary Form
(Modified: October 14, 1998)

EXCLUSIVITY SUMMARY FOR NDA # 20-764

SUPPL # SE1-001

Trade Name: Lamictal Chewable Dispersible Tablets

Generic Name: lamotrigine

Applicant Name: Glaxo Wellcome

HFD #: HFD-120

Approval Date If Known: _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?
YES / ☐ / NO / ☒ /

b) Is it an effectiveness supplement?
YES / ☒ / NO / ☐ /

If yes, what type? (SE1, SE2, etc.) SE1

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / ☒ / NO / ☐ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

Form OGD-011347

cc: Original NDA Division File HFD-93 Mary Ann Holovac

- d) Did the applicant request exclusivity?
YES / X / NO / /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

With the original submission of NDA 20-764/S-001, on 9/4/98, Glaxo Wellcome requested three years of exclusivity from the date of approval of Lamictal as monotherapy for the treatment of partial seizures in adults with epilepsy. [For completeness, a copy of the 9/4/98 request is attached to the end of this exclusivity summary.]

- e) Has pediatric exclusivity been granted for this Active Moiety?
YES / / NO / X /

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO - please indicate as such)

YES / / NO / X /

If yes, NDA # . Drug Name .

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES / / NO / X /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

APPEARS THIS WAY
ON ORIGINAL

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / X / NO / /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#: NDA 20-241/Lamictal (lamotrigine) Tablets
NDA 20-764/Lamictal (lamotrigine) Chewable Dispersible Tablets

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES / / NO / X /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS.

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations?

(The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) **If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a).** If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / X / NO / /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / / NO / /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8.**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / / NO / /

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / / NO / /

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES / ☐ / NO / ☐ /

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES / ☐ / NO / ☒ /

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

(b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES / ☐ / NO / ☒ /

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study US 30/31

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1: Study US 30/31

YES / ☒ / NO / ☐ / Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Not Applicable.

Investigation #1: YES / ☐ / Explain _____ NO / ☐ / Explain _____

Investigation #2: YES / ☐ / Explain _____ NO / ☐ / Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES / ☐ / NO / ☒ /

If yes, explain: _____

Signature of Preparer: _____

/S/

Date: 12/23/98

Title: _____

Regulatory Management Officer

Signature of Office/Division Director

Signature: _____

/S/

Date: 12/23/98

cc:

Original NDA

Division File

HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL